a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, comprising a framework region derived from the heavy chain of the human I2R antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

76. **(NEW)** The humanized immunoglobulin of any one of claims 1 or 10 which binds to human B7-2 with an affinity of about $1x10^9$ M^{-1}.--

REMARKS

Claims 1-40, 46, 49, and 50 were under consideration in the instant application. Claims 13-14, 16-20, 22, 26, 29, 37, and 49-50 have been cancelled without prejudice herein. Claims 1-2, 9-31, 33-34, 36-38, 49, and 46 have been amended. New claims 64-76 have been added. Accordingly, claims 1-12, 15, 21, 23-25, 27-28, 30-36, 38-40, 46, and 64-76 are currently under examination. Support for the amendments to the claims can be found in the specification and/or the claims as previously pending. Support for new claims 64-76 can be found in the specification and/or the claims as previously pending. Specific support for new claim 76 can be found in the specification as filed at page 43, lines 11-15.

Applicant submits herewith a "Version with Markings to Show Changes Made," which indicates the specific amendments made to the claims and the specification.

No new matter has been added. Amendment and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite prosecution. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Formal Drawings

The Examiner has objected to the drawings, which fail to comply with 37 CFR 1.142(b). Applicants will submit substitute formal drawings which comply with 37 CFR 1.142(b) upon indication from the Patent Office that the pending claims are in condition for allowance.

Specification

The Examiner has required that the application be reviewed and all spelling, TRADEMARKS, and like errors be corrected. Applicants have made every effort to detect and correct such errors in the application. Applicants submit that the trademarks known to Applicants are capitalized, that the proprietary nature of the marks has been respected, and that every effort has been made to prevent their use in any manner which might adversely affect their value as trademarks.

Rejection of Claims 9, 11-15, 17-23, 25-27, 29, 31, 34, and 37-40 Under 35 U.S.C. §112, First Paragraph

Claims 9, 11-15, 17-23, 25-27, 29, 31, 34, and 37-40 have been rejected under 35 U.S.C. §112, first paragraph, because, "As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell lines/hybridomas which produce these antibodies." This rejection is traversed in part and met in part.

Claims 13-14, 17-20, 22, 26, 29, and 37 have been cancelled without prejudice. Accordingly, the rejection of these claims under 35 U.S.C. §112, first paragraph is rendered moot.

With respect to claim 15, the specification discloses, at least at page 13, lines 12-17, that the cell line CRL-12524 was deposited with the ATCC, 10801 University Boulevard, Manassas, VA 02110-2209, on May 5, 1998. In light of the deposit details disclosed in the specification, Applicants submit that there is sufficient disclosure of the CRL-12524 cell line.

With respect to claims which recite the term 3D1, Applicants submit that this antibody is known in the art (Freeman et al., U.S. Patent No. 6,084,067, cited by the Examiner). Moreover, as set forth in that patent, a hybridoma which produces this antibody is available from ATCC (Accession No. HB11686). With respect to claims which recite the terms H2F and I2R, the H2F and I2R antibodies also known in the art. These antibodies are disclosed in Manheimer -Lory A. et al. (1991) J. Exp. Med. 174:1639-52, which is a reference disclosed at page 36, lines 14-17 of the instant specification. Thus, these antibodies are also known and available to the public

In light of the comments above, Applicants submit that all of the elements of claims 9, 11-12, 15, 21, 23, 25, 27, 31, 34, and 38-40, as well as all of the new claims, are known and readily available to the public or obtainable by a repeatable method set forth in the specification. Accordingly, Applicants respectfully request that the rejection of these claims be reconsidered and withdrawn.

Rejection of Claims 5, 11-15, 17-29, 31, 34, and 37-40 Under 35 U.S.C. §112, Second Paragraph

Claims 5, 11-15, 17-29, 31, 34, and 37-40 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner has itemized a number of different reasons for the rejection which are set forth below.

A) Claims 11-15, 17-23, 25-27, 29, 31, 34, and 37-40 have been rejected as being indefinite in the recitation of "3D1", "H2F", and "I2R" antibodies because their

characteristics are not known. Applicants respectfully traverse this rejection. Applicants submit that the 3D1 antibody is described in the specification at least at page 17, lines 1-6, and the H2F and I2R antibodies are described in the specification at least at page 36, lines 14-17. Moreover, as set forth above, these antibodies are also known in the art. For example, 3D1 is disclosed in United States Patent 6,084,067 and the H2F and I2R antibodies are disclosed in Manheimer -Lory A. et al. (1991) J. Exp. Med. 174:1639-52. Accordingly, references to these antibodies are not indefinite.

Claims 13-14, 17-20, 22, 26, 29, and 37 have been cancelled without prejudice. Accordingly, the rejection of claims 13-14, 17-20, 22, 26, 29, and 37 under 35 U.S.C. §112, second paragraph is rendered moot.

Applicants point out that claim 15 does not recite any of the terms "3D1", "H2F", or "I2R". Accordingly, Applicants respectfully request that the rejection of claim 15 under 35 U.S.C. §112, second paragraph be withdrawn.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 11-12, 21, 23, 25, 27, 31, 34, and 38-40 under 35 U.S.C. §112, second paragraph.

B) Claim 5 has been rejected as being indefinite in the recitation of amino acid residue substitutions without a base sequence to indicate the appropriate amino acid residues. Applicants submit that the amendment to claim 5 to clarify that the amino acid changes were made in the IgG2 constant region. Applicants respectfully request reconsideration and withdrawal of claim 5 under 35 U.S.C. §112, second paragraph.

C) Claims 24 and 28 have been rejected as being indefinite over the recitation of "stringent conditions". Applicants respectfully traverse this rejection. Applicants submit that the term "stringent hybridization conditions" was an art recognized term at the time of the invention, and therefore one of skill in the art would have known what Applicants regarded as the invention with respect to this term. Accordingly, Applicants submit that claims 24 and

28 are definite and respectfully request reconsideration and withdrawal of the rejection of claims 24 and 28 under 35 U.S.C. §112, second paragraph.

Rejection of Claims 1-4, 6-40, 46, 49, and 50 Under 35 U.S.C. §102(e)

Claims 1-4, 6-40, 46, 49, and 50 have been rejected under 35 U.S.C. §102(e) as being anticipated by Freeman et al. (U.S. Patent No. 6,084,067). Applicants point out that the text of the Office Action recites "Claims 1-4, 640, 46, 49, 50" as being rejected. As there is no pending claim 640, Applicants will respond to the instant rejection as if it had been made with respect to claims 6-40. This rejection is respectfully traversed.

Applicants have cancelled claims 13-14, 16-20, 22, 26, 29, 37, and 49-50. Accordingly, the rejection of claims 13-14, 16-20, 22, 26, 29, 37, and 49-50 is rendered moot. Applicants respectfully traverse the rejection of claims 1-4, 6-13, 21, 23-25, 27-28, 30-36, 38-40, and 46, as well as all new claims, under 35 U.S.C. §102(e).

The pending claims are directed to a humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising an antigen binding region of non-human origin and at least a portion of an immunoglobulin of human origin wherein the antigen binding region comprises ***a heavy chain derived from the I2R antibody or a light chain derived from the H2F antibody***. The claims are further directed to a humanized immunoglobulin having binding specificity for B7-2 which humanized immunoglobulin is ***derived from the cell line deposited with the ATCC®, Accession No. CRL-12524***. The pending claims are further directed to a humanized immunoglobulin light chain having binding specificity for B7-2 comprising CDR1, CDR2 and CDR3 of the light chain of the murine 3D1 antibody, ***and a human light chain framework region derived from the light chain of the human H2F antibody***. The pending claims are yet further directed to an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

a) ***SEQ ID NO:7***,

b) a nucleotide sequence encoding the amino acid sequence of ***SEQ ID NO:8***,

c) the nucleic acid sequence of a nucleic acid molecule which hybridizes to the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and

d) a nucleotide sequence which is the complement of the nucleotide sequence according to a) or b).

The pending claims are still further directed to a humanized immunoglobulin heavy chain specific for B7-2 comprising CDR1, CDR2 and CDR3 of the heavy chain of the murine 3D1 antibody, ***and a human heavy chain framework region derived from the heavy chain of the human I2R antibody***. The pending claims are further directed to an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

a) ***SEQ ID NO: 5***,

b) a nucleotide sequence encoding the amino acid sequence of ***SEQ ID NO:6***,

c) the nucleotide sequence of a nucleic acid molecule which hybridizes to the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and

d) a nucleotide sequence which is the complement of the nucleotide sequence according to a) or b).

The pending claims are yet further directed to an expression vector comprising a fused gene encoding a humanized immunoglobulin light chain, said gene comprising a nucleotide sequence encoding a CDR derived from a light chain of a nonhuman antibody having binding specificity for B7-2 ***and a framework region derived from the light chain of the human H2F antibody***. The pending claims are still further directed to an expression vector comprising a fused gene encoding a humanized immunoglobulin heavy chain, said gene comprising a nucleotide sequence encoding a CDR derived from a heavy chain of a

nonhuman antibody having binding specificity for B7-2 ***and a framework region derived from the heavy chain of the human I2R antibody***. The pending claims are still further directed to a fused gene encoding a humanized immunoglobulin light chain comprising:

a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, ***comprising a framework region derived from the light chain of the human H2F antibody***; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

The pending claims are still further directed to a fused gene encoding a humanized immunoglobulin heavy chain comprising:

a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, ***comprising a framework region derived from the heavy chain of the human I2R antibody***; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

The pending claims all require that the humanized molecule comprise specific regions derived from a specific human antibody molecule, be derived from a specific cell line, or comprise a specific nucleotide sequence.

As admitted by the Examiner, Freeman et al. does not disclose the specific sequences recited in the claims. Freeman et al. further does not disclose the use of either the H2F or the I2R antibodies from which to derive the framework regions for the humanized antibodies of the instant invention. It is well established that in order for a reference to anticipate a claim, the reference must disclose each and every element of the claim. All of pending claims 1-4, 6-13, 21, 23-25, 27-28, 30-36, 38-40, and 46, as well as all new claims, recite either a specific SEQ ID NO, or require that a portion of the humanized antibody be derived from the H2F antibody, or the I2R antibody, none of which is disclosed in Freeman et al.

Accordingly, the Freeman reference does not anticipate the claims and Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4, 6-13, 21, 23-25, 27-28, 30-36, 38-40, and 46 under 35 U.S.C. §102(e).

Applicants respectfully traverse the rejection of claim 15 under 35 U.S.C. §102(e). Claim 15 is drawn to a humanized immunoglobulin derived from the cell line deposited with the ATCC, Accession No. CRL-12524. This cell line is not disclosed in Freeman et al. Accordingly, the claim is not anticipated by that reference and Applicants respectfully request reconsideration and withdrawal of the rejection of claim 15 under 35 U.S.C. §102(e).

Rejection of Claims 1-4, 6-40, 46, 49, and 50 Under 35 U.S.C. §103

Claims 1-40, 46, 49, and 50 have been rejected under 35 U.S.C. §103 as being obvious over Freeman et al. (U.S. Patent 6,084,067) in view of art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof. According to the Examiner, "the modifications of '3D1' antibody were designed on known parameters, techniques and computer programs (ABMOD and ENCODE) at the time the invention was made..., including modifications to the framework regions to allow the recombinant antibodies to maintain substantial affinity to B7-2." Applicants respectfully traverse this rejection.

Claims 13-14, 16-20, 22, 26, 29, 37, and 49-50 have been cancelled without prejudice. Accordingly, the rejection of these claims under 35 U.S.C. §103 is rendered moot.

The pending claims are not obvious over Freeman et al. To establish a *prima facie* case of obviousness for the claimed invention, there must have been some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in the manner proposed by the Examiner. Second, there must have been a reasonable expectation of success at the time the invention was made. Finally, the prior art reference (or

references when combined) must teach or suggest all the claim limitations. See M.P.E.P. 2143. The prior art must suggest "to those of ordinary skill in the art that they ***should*** make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable expectation of success ***must be founded in the prior art, not in the applicant's disclosure*** (emphasis added)." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

The subject matter of the pending claims is set forth above. The pending claims all require that the humanized molecule comprise specific regions derived from a specific human antibody molecule, be derived from a specific cell line, or comprise a specific nucleotide sequence. These human antibody molecules and nucleotide sequences required by the present claims are not taught in the Freeman reference. Therefore, the reference cited by the Examiner fails to teach or suggest all the elements of the claims as required by MPEP 2143.

Moreover, the selection of these specific human antibodies to derive the heavy and light chain framework regions out of all the possible human antibodies possible would not have been obvious to one of skill in the art at the time the invention was made. Furthermore, it would not have been obvious to one of skill in the art to select two different antibodies from which to derive the heavy and light chain variable region frameworks. As described in the specification at page 36, line 21 to page 37, line 3, "Normally the heavy chain and light chain ***from the same human antibody*** are chosen to provide the framework sequences, so as to reduce the possibility of incompatibility in the assembling of the two chains. In this case, the inventors found that the I2R antibody shows a high homology to the 3D1 heavy and light chains and thus, was chosen to provide the framework for the initial humanized antibody model. The 3D1 light chain variable region, however, shows a significantly higher homology to the H2F framework compared to any others, including I2R. Therefore, H2F was chosen instead to provide the framework for the humanized 3D1 light chain variable region, while I2R was selected to provide the framework for the heavy chain variable

region." The selection of these specific human antibodies was not obvious in view of the cited art.

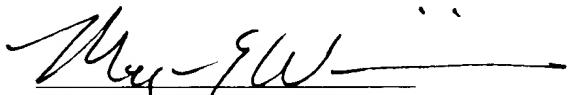
Applicants respectfully submit that the Examiner has failed to make a prima facie showing that the present invention as a whole would have been obvious to one of skill in the art at the time the invention was made. Accordingly, Applicant's respectfully request reconsideration and withdrawal of the rejection of claims 1-2, 15, 21, 23-25, 27, 28, 30-36, 38-40, and 46 under 35 U.S.C. §103.

SUMMARY

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested.

If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the examiner is urged to call Applicants' attorney at (617) 227-7400.

Respectfully submitted,



Megan E. Williams, Esq.
Registration No. 43,270
Attorney for Applicants

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

Dated: April 10, 2001

Version With Markings to Show Changes Made

1. **(Amended)** A humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising an antigen binding region of non-human origin and at least a portion of an immunoglobulin of human origin wherein the antigen binding region comprises a heavy chain derived from the I2R antibody or a light chain derived from the H2F antibody.

2. **(Amended)** The humanized immunoglobulin of Claim 1, wherein the portion of an immunoglobulin of human origin is derived from a human constant region.

3. The humanized immunoglobulin of Claim 2, wherein the human constant region comprises an IgG constant region.

4. The humanized immunoglobulin of Claim 3, wherein the human constant region contains a mutation capable of reducing the effector function of the immunoglobulin.

5. **(Amended)** The humanized immunoglobulin of Claim 4, wherein the human constant region comprises an IgG2 constant region and a Valine amino acid at position 234 of the IgG2 constant region is substituted with Alanine and/or a Glycine amino acid at position 237 of the IgG2 constant region is substituted with Alanine.

6. The humanized immunoglobulin of Claim 3, wherein the IgG constant region is selected from the group consisting of an IgG4 constant region and an IgG2 constant region.

7. The humanized immunoglobulin of Claim 1, wherein the antigen binding region is of rodent origin.

8. The humanized immunoglobulin of Claim 1, wherein the antigen binding region comprises a complementarity determining region of rodent origin, and the portion of an immunoglobulin of human origin is derived from a human framework region.

9. **(Amended)** The humanized immunoglobulin of Claim 8, wherein the complementarity determining region is derived from the 3D1 monoclonal antibody.

10. **(Amended)** The humanized immunoglobulin of claim 9, further ~~having binding specificity for B7-2,~~ comprising a constant region of human origin, wherein the heavy chain comprises a variable region of SEQ ID NO:6 and the light chain comprises a variable region of SEQ ID NO:8 ~~and an antigen binding region, wherein said antigen binding region comprises :~~

~~a) a complementarity determining region derived from an antibody of rodent origin that binds to B7-2, and~~

~~b) a framework region derived from human origin~~.

11. **(Amended)** The humanized immunoglobulin of any one of Claims 1 or 10, wherein said immunoglobulin can compete with the murine 3D1 antibody for binding to B7-2.

12. **(Amended)** The humanized immunoglobulin of Claim 11, wherein the ~~antigen binding region comprises a light chain and a heavy chain, said~~ light and heavy chains each ~~having~~ have three complementary determining regions derived from the 3D1 antibody.

~~13. The humanized immunoglobulin of Claim 12, wherein the framework region of the antigen binding region of the light chain is derived from the light chain of the H2F antibody.~~

~~14. The humanized immunoglobulin of Claim 13, wherein the framework region of the antigen binding region of the heavy chain is derived from the heavy chain of the human I2R antibody.~~

15. **(Amended)** A humanized immunoglobulin having binding specificity for B7-2 which humanized immunoglobulin is derived from the cell line deposited with the ATCC®, Accession No. CRL-12524.

~~16. A humanized immunoglobulin having binding specificity for B7-2 comprising a heavy chain and a light chain,~~

~~the light chain comprising a complementarity determining region derived from an antibody of non-human origin which binds B7-2 and a framework region derived from a light chain of human origin, and~~

~~the heavy chain comprising a complementarity determining region derived from an antibody of non-human origin which binds B7-2 and a framework region derived from a heavy chain of human origin.~~

~~17. The humanized immunoglobulin of Claim 16, wherein the immunoglobulin can compete with murine 3D1 for binding to B7-2.~~

~~18. The humanized immunoglobulin of Claim 16, wherein the light chain comprises three complementarity determining regions derived from the light chain of the 3D1 antibody, and the heavy chain comprises three complementarity determining regions derived from the heavy chain of the 3D1 antibody.~~

~~19. The humanized immunoglobulin of Claim 16, wherein the light chain of human origin is the light chain of the H2F antibody.~~

~~20. The humanized immunoglobulin of Claim 16, wherein the heavy chain of human origin is the human I2R antibody.~~

21. **(Amended)** A humanized immunoglobulin light chain having binding specificity for B7-2 comprising CDR1, CDR2 and CDR3 of the light chain of the murine 3D1 antibody, and a human light chain framework region derived from the light chain of the human H2F antibody.

~~22. The humanized immunoglobulin light chain of Claim 21, wherein the human framework region is derived from the light chain of the H2F antibody.~~

23. **(Amended)** The humanized immunoglobulin light chain of Claim ~~22~~ 21, wherein the light chain comprises a variable region of SEQ ID NO: 8.

24. **(Amended)** An isolated nucleic acid molecule comprising a ~~nucleic acid~~ nucleotide sequence selected from the group consisting of:

a) SEQ ID NO:7,

b) a ~~nucleic acid~~ nucleotide sequence encoding the amino acid sequence of SEQ ID NO:8,

c) the nucleic acid sequence of a nucleic acid molecule which hybridizes to the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and

d) a ~~nucleic acid~~ nucleotide sequence which is the complement of the ~~nucleic acid~~ nucleotide sequence according to a) or b).

25. **(Amended)** A humanized immunoglobulin heavy chain specific for B7-2 comprising CDR1, CDR2 and CDR3 of the heavy chain of the murine 3D1 antibody, and a human heavy chain framework region derived from the heavy chain of the human I2R antibody.

~~26. The humanized immunoglobulin heavy chain of Claim 25, wherein the human framework region is derived from the heavy chain of the human I2R antibody.~~

27. **(Amended)** The humanized immunoglobulin heavy chain of Claim ~~26~~ 25, wherein the heavy chain comprises a variable region of SEQ ID NO:6.

28. **(Amended)** An isolated nucleic acid molecule comprising a ~~nucleic acid~~ nucleotide sequence selected from the group consisting of:

a) SEQ ID NO: 5,

b) a ~~nucleic acid~~ nucleotide sequence encoding the amino acid sequence of SEQ ID NO:6,

c) the nucleotide sequence of a nucleic acid molecule which hybridizes to the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and

d) a ~~nucleic acid~~ nucleotide sequence which is the complement of the ~~nucleic acid~~ nucleotide sequence according to a) or b).

~~29. A humanized immunoglobulin which specifically binds to B7-2 comprising:~~

~~a) a humanized light chain comprising three light chain complementarity determining regions from the mouse 3D1 antibody and a light chain variable region framework sequence from a human immunoglobulin light chain, and~~

~~b) a humanized heavy chain comprising three light chain complementarity determining regions from the mouse 3D1 antibody and a heavy chain variable region framework sequence from a human immunoglobulin heavy chain.~~

30. **(Amended)** An expression vector comprising a fused gene encoding a humanized immunoglobulin light chain, said gene comprising a nucleotide sequence encoding a CDR derived from a light chain of a nonhuman antibody having binding specificity for B7-2 and a

framework region derived from ~~a light chain of human origin~~ the light chain of the human H2F antibody.

31. **(Amended)** The expression vector of Claim 30, wherein the nonhuman antibody is the murine 3D1 antibody.

32. A host cell comprising the expression vector of Claim 30.

33. **(Amended)** An expression vector comprising a fused gene encoding a humanized immunoglobulin heavy chain, said gene comprising a nucleotide sequence encoding a CDR derived from a heavy chain of a nonhuman antibody having binding specificity for B7-2 and a framework region derived from ~~a heavy chain of human origin~~ the heavy chain of the human I2R antibody.

34. **(Amended)** The expression vector of Claim 33, wherein the nonhuman antibody is the murine 3D1 antibody.

35. A host cell comprising the expression vector of Claim 33.

36. **(Amended)** A host cell comprising at least one nucleic acid molecule encoding the humanized immunoglobulin of Claim 1.

~~37. A host cell comprising a first recombinant nucleic acid encoding a humanized immunoglobulin light chain and a second recombinant nucleic acid encoding a humanized immunoglobulin heavy chain, said first nucleic acid comprising a nucleotide sequence encoding a CDR derived from the light chain of murine 3D1 antibody and a framework region derived from a light chain of human origin; and said second nucleic acid comprising a nucleotide sequence encoding a CDR derived from the heavy chain of murine 3D1 antibody and a framework region derived from a heavy chain of human origin.~~

38. **(Amended)** A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim ~~37~~ 36 under conditions appropriate for expression of a humanized immunoglobulin, wherein humanized immunoglobulin chains are expressed and a humanized immunoglobulin is produced.

39. The method of Claim 38, further comprising the step of isolating the humanized immunoglobulin.

40. **(Amended)** A fused gene encoding a humanized immunoglobulin light ~~or heavy~~ chain comprising:

b) a first nucleic acid ~~sequence~~ molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, comprising a framework region derived from the light chain of the human H2F antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

46. **(Amended)** A pharmaceutical composition comprising the antibody of any one of Claims 1 or 10, and a pharmaceutically acceptable carrier.

~~49. A method of making a humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising an antigen binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin, comprising the steps of:~~

~~a) determining the complementarity determining regions of an antibody of nonhuman origin which has binding specificity for B7-2;~~

~~b) obtaining a human obtaining a human antibody having a framework region amino acid sequence suitable for grafting of the complementarity determining regions determined in (a), and~~

~~c) grafting the complementarity determining regions of (a) into the framework region of the human antibody of (b),~~

~~wherein a humanized immunoglobulin having binding specificity for B7-2 is made.~~

~~50. The method of Claim 49, wherein the antibody of nonhuman origin is of murine origin.~~

64. **(NEW)** An expression vector comprising a fused gene encoding a humanized immunoglobulin light chain, said gene comprising the nucleotide sequence of claim 24.

65. **(NEW)** A host cell comprising the expression vector of claim 64.

66. **(NEW)** An expression vector comprising a fused gene encoding a humanized immunoglobulin heavy chain, said gene comprising the nucleotide sequence of claim 28.

67. **(NEW)** A host cell comprising the expression vector of claim 66.

68. **(NEW)** The humanized immunoglobulin of Claim 10, wherein the human constant region comprises an IgG constant region.

69. **(NEW)** The humanized immunoglobulin of Claim 68, wherein the human constant region contains a mutation capable of reducing the effector function of the immunoglobulin.

70. **(NEW)** The humanized immunoglobulin of Claim 69, wherein the human constant region comprises an IgG2 constant region and a Valine amino acid at position 234 of the IgG2 constant region is substituted with Alanine and/or a Glycine amino acid at position 237 of the IgG2 constant region is substituted with Alanine.

71. **(NEW)** The humanized immunoglobulin of Claim 68, wherein the IgG constant region is selected from the group consisting of an IgG4 constant region and an IgG2 constant region.

72. **(NEW)** A host cell comprising at least one nucleic acid molecule encoding the humanized immunoglobulin of Claim 10.

73. **(NEW)** A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim 72 under conditions appropriate for expression of a humanized immunoglobulin, wherein humanized immunoglobulin chains are expressed and a humanized immunoglobulin is produced.

74. **(NEW)** The method of Claim 73, further comprising the step of isolating the humanized immunoglobulin.

75. **(NEW)** A fused gene encoding a humanized immunoglobulin heavy chain comprising:

a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, comprising a framework region derived from the heavy chain of the human I2R antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

76. **(NEW)** The humanized immunoglobulin of any one of claims 1 or 10 which binds to human B7-2 with an affinity of about $1x10^{9}$ M^{-1}.